

REMARKS

This paper is being filed in response to the Office Action dated December 16, 2003 that was issued in connection with the above-identified patent application. Applicants enclose herewith a Petition for Extension of Time pursuant to 37 C.F.R. §1.136(a) and the fee required under 37 C.F.R. §1.17(a)(1). Applicants respectfully request reconsideration of the instant application in view of the amendments and remarks presented herein.

Claims 1-35 are pending. Claims 1-28 and 31-35 have been cancelled. Claim 29 has been amended. Claims 36-48 have been added. Therefore, upon entry of the instant amendment, claims 29-30 and 36-48 will be pending.

The amendments to claim 29 are fully supported by the application as filed at, for example, paragraphs [0011] and [0034] and, therefore, do not constitute new matter.

New claims 36-46 are fully supported by the application as filed at, for example, original claims 2-11 and 17. New claim 47 is fully supported by the application as filed at, for example, paragraphs [0032] and original claims 15-16. New claim 48 is fully supported by the application as filed at, for example, the last sentence of paragraph [0017] and original claim 28. Accordingly, new claims 36-48 do not constitute new matter.

An objection has been raised against the specification. Specifically, the Examiner has alleged that there is no section of the specification that is titled "BRIEF DESCRIPTION OF THE DRAWINGS." Applicants traverse this objection and assert that while not marked as such, a section briefly describing the drawings was present in the application as filed at paragraph [0018] et seq. Applicants have amended the specification to insert an appropriate heading and, therefore, respectfully request withdrawal of this objection.

Claims Are Clear and Definite

Claims 29 and 30 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. The Examiner has alleged that claim 29 is vague and indefinite for reciting the terms "preferably." Applicants traverse this rejection and assert that claim 29, as amended herein, does not recite "preferably."

Claim 29 has also been rejected as allegedly indefinite for reciting the phrase "phosphorylated at positions Y and Z" in part (b). The Examiner has alleged that it is unclear how a substrate already phosphorylated at position Y in step (a) could be phosphorylated again in step (b). Applicants traverse this rejection and assert that claim 29, as amended herein is clear and definite. Claim 29 has been amended to recite "phosphorylated at position Z."

In addition, claim 29 has been rejected as allegedly indefinite for reciting the phrase "a peptide or protein which is phosphorylated at the Y and Z position" in part (c). The Examiner has alleged that it is unclear whether the antibody is specific for the kinase substrate protein or peptide of part (a) or if it is specific for another peptide or protein phosphorylated at the Y and Z position. The Examiner has further alleged that it is unclear whether the antibody binds to the Y and Z position of the protein or peptide or the amino acid.

Applicants traverse these rejections and assert that claim 29, as amended herein, is clear and definite. Applicants assert that it would have been clear to one of ordinary skill in the art that the antecedent for the phrase "a peptide or protein" in part (c) is the kinase substrate peptide or protein in (a). Nevertheless, since it does not alter the scope of the claim in any way, Applicants have amended part (c) to recite "the kinase substrate peptide or protein."

Applicants note that the invention contemplates that some modulators may be sufficiently potent kinase inhibitors that, even though reaction conditions otherwise permit

phosphorylation at the Z position, little or no detectable bis-phosphorylated product is formed due to the presence of the modulator. *See e.g.* Examples 6-7. Applicants assert that claims 29, as amended herein, and 48 embrace this possibility in paragraph (c) in the expression "to **permit** phosphorylation" (emphasis added). Therefore, this amendment does not constitute the surrender of this subject matter.

Claims Are Not Anticipated by Davis I

Claims 29-30 have been rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent Publication No. 2003/0023990 by Davis et al. (hereinafter "Davis I"). The Examiner has alleged that Davis I discloses in vitro assays that measure protein kinase activity using protein substrates and ATP. The Examiner has also alleged that Davis I discloses activation of JNK protein kinases by dual phosphorylation on threonine and tyrosine residues in subdomain VIII. In addition, the Examiner has alleged that Davis I discloses that molecules that interfere with kinase activation may be identified by measuring activation in the presence and absence of candidate molecules. The Examiner has further alleged that Davis I discloses that kinase activation can be immunologically probed using antibodies that bind the phosphorylated threonine and tyrosine. According to the Examiner, Davis I's disclosure of phosphorylation at the Y position allegedly reads on instant claims 29-30 since the instant claims allegedly do not provide a sequence of steps for substrate phosphorylation. Davis I also allegedly reads on instant claims 29-30 since it is allegedly unclear whether the Y position is phosphorylated once or twice.

Applicants traverse this rejection and assert that claims 29-30 are patentable over Davis I. For a reference to anticipate, it must teach each and every limitation of the claims. *See e.g. Structural Rubber Products Co. v. Park Rubber Co.*, 749 F.2d 707, 715-716 (Fed. Cir.

1984). Davis I fails to anticipate the instant claims since it fails to teach the recited substrate or antibody.

Claim 29, as amended herein, recites “Y = phospho-tyrosine, phospho-threonine or phospho-serine.” By contrast, the only kinase substrates recited by Davis I are ATF2 and Elk-1. *See* Davis I, paragraph [0160]. Since these proteins are not inherently pre-phosphorylated and Davis I fails to teach pre-phosphorylation of the kinase substrate peptide or protein described, Davis I fails to anticipate the instant claims.

Not only does an reference have to teach each and every element of a claimed invention in order to anticipate the claimed invention, it must also teach those elements in the same detail as claimed. *See* MPEP § 2131, *citing Richardson v. Suzuki Motor Co.*, 868 F.2d 1226 (Fed. Cir. 1989)(“The identical invention must be shown in as complete detail as contained in the ... claim”). Claim 29 recites “an antibody having a specificity to the kinase **substrate** peptide or protein which is phosphorylated at the Y **and** Z positions” (emphasis added). Davis I only discloses two types of antibodies. In the first instance, Davis I refers generally to commercially available antibodies that may bond phosphorylated substrates. *See* Davis I, paragraph [0161]. The other antibody taught by Davis I does not recognize the **substrate** at all, but rather the phosphorylated form of c-Jun N-terminal **kinase** (JNK). *See* Davis I, paragraph [0164]. In neither case does Davis I specifically disclose the use of an antibody having a specificity to a bis-phosphorylated kinase **substrate** peptide. Consequently, Davis I fails to teach each and every element of the claimed invention. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims Are Not Obvious over Davis II in View of Davis I

Claims 29-30 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over International Patent Publication No. WO 96/36642 by Davis et al. (hereinafter “Davis II”) in view of Davis I. The Examiner has alleged that Davis II discloses reagents and methods for identifying agents that modulate MKK activity. The Examiner has acknowledged that Davis II fails to teach an antibody that is specific for a peptide or protein that has been phosphorylated and the Y and Z position. However, the Examiner has alleged that Davis I discloses that kinase activation can be immunologically probed using antibodies that bind the phosphorylated threonine and tyrosine. Accordingly, the Examiner alleged that it would have been obvious to one of ordinary skill in the art to incorporate the antibodies of Davis I in the method of Davis II. The Examiner has alleged that Davis II’s disclosure of phosphorylation at the Y position reads on instant claims 29-30 since the instant claims allegedly do not provide a sequence of steps for substrate phosphorylation.

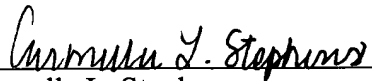
Applicants traverse this rejection and assert that claims 29-30 are patentable over Davis II in view of Davis I. As noted above, Davis I fails to teach or suggest a kinase substrate wherein Y = phospho-tyrosine, phospho-threonine or phospho-serine.” Davis II, which relates to the identification and isolation of human mitogen-activated protein kinase kinases, also fails to teach or suggest such substrates. In addition, as the Examiner has acknowledged, since Davis II only discloses [³²P] incorporation assays, it fails to teach or suggest an antibody having a specificity to a bis-phosphorylated kinase substrate peptide. Therefore, Davis I and Davis II, whether considered alone or in combination, fail to teach or suggest the instant claimed invention. Applicants, therefore respectfully request withdrawal of this rejection.

In conclusion, since none of the cited prior art teaches or suggests either the pre-phosphorylated substrate or an antibody with specificity for a bis-phosphorylated kinase substrate, Applicants believe the claims of the instant application are patentable over the cited prior art. Accordingly, Applicants respectfully request prompt favorable action.

Applicants enclose herewith the fee required under 37 C.F.R. §1.17(a)(1). Applicants do not believe that any additional fees are required with this Response. Nevertheless, the Commissioner is hereby authorized to charge any required fees not otherwise enclosed herewith to Deposit Account No. 02-4377. Two copies of a Fee Transmittal sheet are enclosed.

Respectfully submitted,

April 16, 2004


Carmella L. Stephens
PTO Reg. No. 41,328
Attorney for Applicants

Guy F. Birkenmeier
PTO Reg. No. 52,622
Agent for Applicants

BAKER BOTTS, L.L.P.
30 Rockefeller Plaza
New York, NY 10112
(212) 408-2500